CE IVD

Precision in Hemostasis

Behnk Elektronik

BE DDimer Turbidimetric Immunoassay

Reagent for quantitative determination of D-Dimer (DD) in human plasma

REF 771500: BU (3 x 7 mL), AC (3 x 4 mL)
CAL (2 x 1 mL), DIL (2 x 7 mL)

| INTENDED USE

This reagent is designated for professional use in laboratory (automated method).
This Latex immunoassay is a quantitative test to determine D-Dimer in citrated human plasma. It can be used to exclude the presence of thrombosis in patients with suspected thrombotic disorders and as an aid in the management of patients with Covid-19 disease.

PRINCIPLE

BE DDimer reagent consists in sub-micron sized polystyrene particles coupled to monoclonal antibodies specific for D-Dimer. When plasma specimen containing D-Dimer is exposed to the reagent, the particles will agglutinate, giving rise to increased light-scattering. This phenomenon leads to an increase of absorbance measured at 400-800 nm which is proportional to the concentration of D-Dimer in the specimen.

GENERALITIES [3-6] [12] [13]

Fibrin fragments containing D-Dimer antigen is always present in plasma because of plasmin degradation.
After an injury or in case of conditions associated with increased haemostatic activity, the D-Dimer concentration increases in plasma.
The determination of D-Dimer concentration is an aid in the diagnosis of thrombosis. Deep vein thrombosis (DVT), pulmonary embolism (PE) and disseminated intravascular coagulation (DIC) are associated with elevated level of D-Dimer.
A negative D-Dimer test result has a high negative predictive value for patient with a suspected thrombotic disorder.
| This test should be used with other clinical and diagnostic information to diagnose and manage patients.
In patients with Covid-19 disease, increasing plasma D-dimer is seen with worsening disease. Markedly elevated D-dimer is a prognostic marker for mortality and can be used as an aid in managing anticoagulant treatment of hospitalized Covid-19 patients.

| REAGENTS

BU **DD BU** Reaction Buffer
Buffer
Sodium azide < 0.1 %, 2-methylisothiazol-3(2H)-one < 0.0015 %

AC **DD AC** Latex Reagent
Polystyrene particles coated with monoclonal antibodies
Buffer
Sodium azide < 0.1 %, 2-methylisothiazol-3(2H)-one < 0.0015 %

EUH208: May produce an allergic reaction.
EUH210: Safety Data Sheet available on request

CAL **DD Cal** DDimer Calibrator
Freeze dried citrated plasma enriched with D-Dimer
Additives of components from bovine plasma
BSA < 4 %
Sodium azide < 0.001 %

Human origin

DIL **DD DIL** Dilution Buffer
For dilution of D-Dimer Calibrator (Standard curve) and plasma of patients.

According to 1272/2008/ EC Regulation, these reagents are not classified as harmful.

SAFETY CAUTIONS [1] [2]

- Refer to current Material Safety Data Sheet available on request or on www.behnk.de
- Each human donor unit used to manufacture this product (vial R3)was tested and found non-reactive for HbsAg, antibody to Hepatitis C and antibody to HIV-1/HIV-2.
- Products from animal origin were approved ante- and postmortem by veterinarians inspection.
- However, no test method can offer complete assurance that infectious agents are absent. All specimens or reagents from biological origin should be handled as potentially infectious, in accordance with good laboratory practices using appropriate precautions.
- Waste disposal: Respect legislation in force in the country.

Any serious incident that has occurred in connection with the device is notified to the manufacturer and the competent authority of the Member State in which the user and/or patient is based.

PREPARATION OF REAGENTS

BU; DIL: Ready for use.
AC: Ready for use; swirl gently the Latex reagent before use to homogenise latex particles.
CAL: Open the vial carefully and add exactly the volume of demineralised water stated on the label without delay.
Cap the vial and let stand for 15 minutes at room temperature (15-25 °C).
Gently agitate until the content is completely dissolved.

| STABILITY AND STORAGE

Unopened vials, stored away from light at 2-8 °C are stable until the expiry date stated on the label.
Stability once opened, free from contamination, **BU, AC** and **DIL**:

- 2-8 °C 8 weeks
- On board Stability (OBS)* 5 days
- Laboratory mode** 7 days
- 15-25 °C 2 weeks

* 18-22 °C
** Laboratory mode = 8 hours on board; 16 hours well capped in the original vial at 2-8 °C.

Stability after reconstitution, free from contamination, **CAL**:

- 2-8 °C 7 days
- 15-25 °C 24 hours

Do not use any reagent after expiry date.

| SAMPLES COLLECTION AND HANDLING [7]

Citrate plasma:
Mix freshly drawn blood with anticoagulant (tri-sodium citrate solution 0.109 M) in a ratio of 1/10. The ratio is essential. Trauma or stasis during blood collection should be avoided.
Inverse immediately after sampling.
The presents of any clots in a specimen is a cause for rejection.
Centrifuge 10 minutes at 3000 g and extract supernatant.

LIMITS [10]

Turbid or opalescent plasma may cause erratic results and should be interpreted with caution: dilute the sample and re-assay.
Patients who have received mouse monoclonal antibodies for diagnosis or therapy may have plasmas containing anti-mouse antibodies (HAMA). Such antibodies may lead to false enhance D-Dimer concentration. The same may occur with Rheumatoid Factor.
For a more comprehensive review of factors affecting this assay, refer to the publication of Young D.S.

MATERIAL REQUIRED BUT NOT PROVIDED

Basic medical analysis laboratory equipment
Coagulation analyzer with turbidimetric detection between 400-800 nm
Demineralised water

REFERENCE RANGE [6] [8] [14] [15]

Plasma: < 200 ng/mL (DDU)
| D-Dimer increases in patients with deep venous thrombosis (DVT), pulmonary embolism, disseminated intravascular coagulation, severe COVID-19 disease, and trauma. D-Dimer increase also during pregnancy and with age.
As there is no international established standard for D-Dimer, the concentration in any given specimen may differ when determined using D-Dimer assays from different manufacturers.
Each laboratory should establish its own reference ranges and cut off levels for the population that it serves.

QUALITY CONTROL

REF 773200: BE DD Trol 1; REF 773201: BE DD Trol 2
Controls are required for checking the accuracy and reproducibility of the results.
The control intervals should be adapted to each laboratory's individual requirements.
Values obtained should fall within the defined limits.
Follow the applicable government regulations and local guidelines for quality control.

PROCEDURE

Automated method on Behnk Thrombolyzer series
Refer to the full detailed application specific to the automated system.
Note:

- Performances and stability data have been validated on Thrombolyzer Compact X (available on request).
- On other automated coagulation analyzer, performances and stability data must be validated by user.

| CALIBRATION [9] [11]

REF 771500: DDimer Calibrator (**DD CAL**) traceable to an In-House Reference Preparation which value was assigned using a working calibrator traceable according to ISO 17511:2020, section 5.6.

- Batch-specific assigned value is indicated in the certificate of analysis (DDU) and on the label of the vial (DDU/FEU).

Automated method on Behnk Thrombolyzer series:

- Perform a calibration with DD CAL using automatic dilutions indicated in the specific application.

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Made in France

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CALCULATION

| DDimer concentration (ng/mL) will be calculated automatically according to calibration curve. The results can be expressed in DDU or FEU, depending on the assigned value entered during calibration.

To convert DDU results in Fibrinogen eq. units (FEU), multiply the result (DDU) by 2.5.

| Samples upper of the measuring range should be manually diluted and re-assayed. No result outside the measuring range should be used for diagnosing or for patient management.

PERFORMANCES

The studies were performed on Thrombolyzer Compact X (all values in DDU).
Precision:

Within run *N = 20*	Level 1	Level 2
Mean (ng/mL DDU)	595	1203
S.D. (ng/mL DDU)	11.2	33.3
CV %	1.9	2.8

Between run *N = 20*	Level 1	Level 2
Mean (ng/mL DDU)	595	1203
S.D. (ng/mL DDU)	6.4	25.9
CV %	1.1	2.2

Detection limit: approx. 98 ng/mL

Measuring range: between 100 (QL) and 3200 ng/mL

Prozone (Hook) effect: tested in the range from 500 to 100 000 ng/mL, no effect.
No result below the Cut off value.

Cut off: 200 ng/mL

Sensitivity: 95 %

Negative Predictive value: 98 %

Comparison with a commercially available reagent (same method) on Thrombolyzer Compact X and Sysmex CA-1500: using 50 specimens between 114 and 3095 ng/mL:
y = 0.95 x r = 0.9742

Interferences:

Turbidity	Negative interference from 290 mg/dL of Triglycerides
Low Molecular weight heparin	No interference up to 100 U/ml
Unfractionated heparin	No interference up to 100 U/ml
Bilirubin	No interference up to 855 µmol/L
Hemoglobin	Negative interference from 1.86 mmol/L

Other substances may interfere with the results (see § Limits)

Calibration Stability: Make a new calibration when changing reagent batch, if quality control results are found out of the established range and after maintenance operations.

REFERENCES

(1) *Occupational Safety and Health Standards; Bloodborne pathogens (29CFR1910.1030) Federal Register July 1, (1998) ; 6, p.267-280*
(2) *Directive du conseil de l'Europe (90/679/CEE) J. O. de la communauté européenne n°L374 du 31.12.1990, p.1-12*
(3) *Heit, J.A. et al. Determinants of plasma fibrin D-Dimer sensitivity for acute pulmonary embolism as defined by pulmonary angiography. Arch Pathol Lab Med, 123:235-239,1999*
(4) *Bounameaux, H., et al. Plasma measurement of D-Dimer as diagnosis aid in suspected venous thromboembolism: an overview. Thromb Haemostas, 71:1-6,1994*
(5) *Pfitzner S.A. et al. Fibrin detected in plasma of patients with disseminated intravascular coagulation by fibrin-specific antibodies consists primarily of high molecular weight factor XIII-cross linked and plasmin-modified complexes partially containing fibrinopeptide A. Thromb Haemostas, 78: 1069-1078, 1997*
(6) *Lindhal T. et al. Clinical evaluation of a diagnosis strategy for deep venous thrombosis with exclusion by low plasma levels of fibrin degradation product D-Dimer. Scan J Lab Invest, 58: 307-316, 1998*
(7) *CLSI Approved Guideline H21-A5*
(8) *Gardiner, C. Et al. An evaluation of rapid D-Dimer assays for the exclusion of deep vein thrombosis. British Journal of Haematology, 128:842-848, 2005*
(9) *Section 5.6 of ISO 17511-Measurement of quantities in biological samples-metrological tracebility of values assigned to calibrators and controls*
(10) *YOUNG D.S., Effect of Drugs on Clinical laboratory Tests, 4th Ed. (1995) p 3-216 to 3-216*
(11) *EN ISO 17511 In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials*
(12) *ROSTAMI, Mehrdad; MANSOURITORGHABEH, Hassan. D-dimer level in COVID-19 infection: a systematic review. Expert review of hematology, 2020, 13.11: 1265-1275.*
(13) *COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed [2022-05-05].*
(14) *BALLEGEER, V., et al. Fibrinolytic response to venous occlusion and fibrin fragment D-dimer levels in normal and complicated pregnancy. Thrombosis and haemostasis, 1987, 58.08: 1030-1032.*
(15) *KARIO, Kazuomi; MATSUO, Takefumi; KOBAYASHI, Hiroko. Which factors affect high D-dimer levels in the elderly?. Thrombosis research, 1991, 62.5: 501-508*

| = Significant modifications

IFU_771500-EN_V03_20230925

Manufacturer	Expiry date	In Vitro Diagnostic	Temperature limitation	Catalogue number	See insert	Batch number	Store away from light	Sufficient for	Dilute with	Demineralized water	Biological hazard

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